Comparison of nWBV and ASF between Dementia Statuses as MRI Visits Increase

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Introduction

People often think that dementia is part of normal aging, but this assumption is not true. Dementia is an impaired ability to remember, problem-solve, and make decisions, which interferes with daily life (Division of Population Health, 2019). Alzheimer's disease destroys brain cells, and it is the most common type of dementia ("What is Alzheimer's disease?", 2024). Over 50 million people worldwide have dementia in 2020, and this number will nearly double every 20 years ("Dementia Statistics", n.d.). The rise of cases leads to the exploration of MRI results of patients with or without dementia. The *INF2178_A4_data.csv* dataset is analyzed to address the fundamental research question: do normalized whole brain volume (nWBV) and Atlas Scaling Factor (ASF) change significantly among demented, converted, and undemented people as they take more MRI scans.

Exploratory Data Analysis

150 patients aged 60 to 98 years took two MRI scans and there is at least a year gap between these two scans. There are 64 demented, 72 undemented, and 14 converted patients. The converted status means the patient was initially undemented, but then changed to demented in the next visit. 2 patients from each dementia status did not participate in the second MRI scan. nWBV is defined as the "percentage of the intracranial cavity occupied by the brain" (Roe et al., 2011). After comparing the medians of nWBV (see Table 1 and Figure 1), it appears that nWBV dropped in the second visit regardless of the dementia status. The nondemented group have the highest median of nWBV in both visits (i.e. 0.747 in the first visit and 0.739 in the second visit). On the contrary, the demented group have the lowest median of nWBV in both visits (i.e. 0.726 in the first visit and 0.708 in the second visit). Research has shown that a small brain volume can lead to poor cognitive performance (Starkman, n.d.). This explains why people with dementia, who suffer the loss of memory and thinking abilities, have a lower nWBV than the other two groups in this study. Although converted patients ultimately have dementia, they did not have dementia throughout the experiment. As a result, their median of nWBV is higher than demented patients. The conversion might also be the reason why they have the largest IQR (0.058) out of the three groups. Only one outlier is found in the demented group during the first visit.

Atlas Scaling Factor is the volume expansion (ASF > 1) or contraction (ASF < 1) required to match the individual to the atlas target (i.e. determinant of the transform matrix) (Buckner et al., 2004). According to Table 2 and Figure 2, the median of ASF in each visit is greater than 1 regardless of the dementia status. This implies that a volume expansion is required to match the patient to the atlas target. In addition, the median of ASF dropped in the second visit for all groups. The converted group almost have the same median in both visits with a minor difference of 0.005. In each visit, the converted group have the highest median (i.e. 1.249 in the first visit and 1.244 in the second visit) and the demented group has the lowest median (i.e. 1.204 in the first visit and 1.184 on the second visit). There is an outlier for the demented group during the second visit.

Dementia Status	Nondemented		Demented		Converted	
Visit	1	2	1	2	1	2
Min	0.666	0.663	0.660	0.646	0.693	0.677
Max	0.837	0.827	0.806	0.791	0.799	0.788
25th percentile	0.725	0.714	0.703	0.694	0.715	0.705
Median	0.747	0.739	0.726	0.708	0.730	0.721
75th percentile	0.770	0.765	0.744	0.737	0.753	0.763
IQR	0.045	0.052	0.041	0.043	0.038	0.058

Table 1. Summary statistics for nWBV.

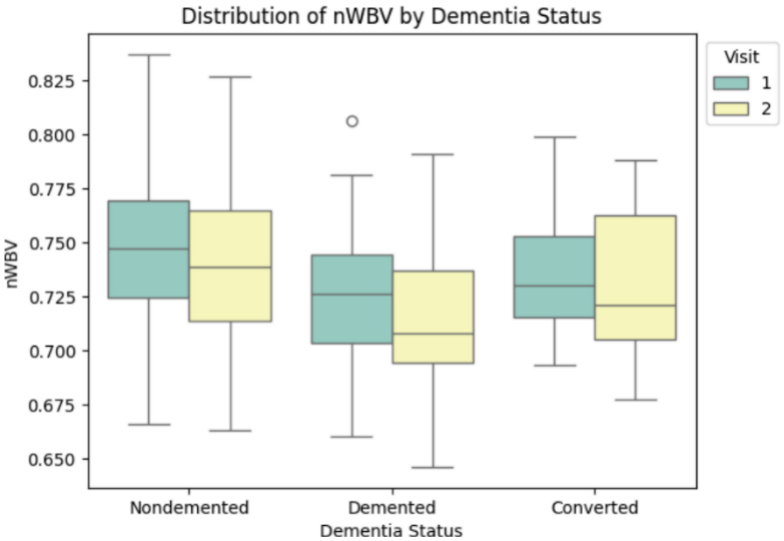

Figure 1. Boxplot of nWBV by visit and dementia status.

Dementia Status	Nondemented		Demented		Converted	
Visit	1	2	1	2	1	2
Min	0.883	0.876	0.897	0.910	1.030	1.019
Max	1.563	1.587	1.525	1.535	1.388	1.376
25th percentile	1.096	1.110	1.132	1.120	1.171	1.134
Median	1.205	1.192	1.204	1.184	1.249	1.244
75th percentile	1.30	1.308	1.299	1.285	1.299	1.328
IQR	0.205	0.199	0.166	0.165	0.129	0.194

Table 2. Summary statistics for ASF.

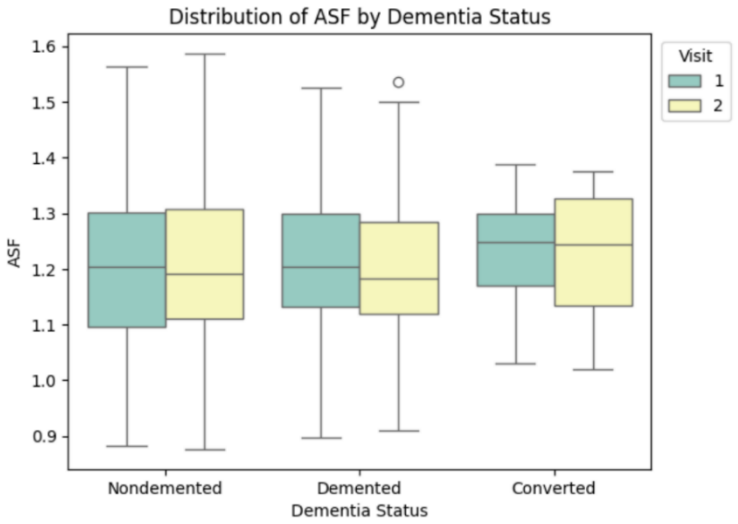

Figure 2. Boxplot of ASF by visit and dementia status.

nWBV Analysis

The Shapiro-Wilk test shown in Table 3 reveals that nWBV is normally distributed for each dementia status and visit at a significance level of $\alpha = 0.05$. The Levene's test shown in Table 4 concludes that the homogeneity of variances between dementia status for each visit is satisfied (p-value > 0.05). Using Mauchly's test in Table 5, the assumption of sphericity holds (p-value > 0.05).

As indicated in the two-way mixed ANOVA summary in Table 6, the F-value for the dementia status is 6.712 and it yields a p-value = 0.002, which is less than the critical threshold of $\alpha = 0.05$. Thus, the means of nWBV differ significantly between dementia statuses. The effect of visits on nWBV is also statistically significant (F-value = 94.251, p-value < 0.001). In other words, there is a statistical difference in nWBV between the first and second visits. The effect size of dementia status is 0.087 and the effect size of visits is 0.401. Hence, the number of visits has a larger effect on nWBV than the dementia status of the patient. With a large p-value of 0.219, there is no significant interaction effect between dementia status and visits, which means the number of visits does not influence nWBV based on the dementia status. These assessments can be supported by the output plot visualized in Figure 3. The nondemented group have the highest mean (0.746 in the first visit and 0.738 in the second visit), whereas the demented group have the lowest mean (0.724 in the first visit and 0.714 in the second visit). Plus, the mean of nWBV is higher for each group during the first visit

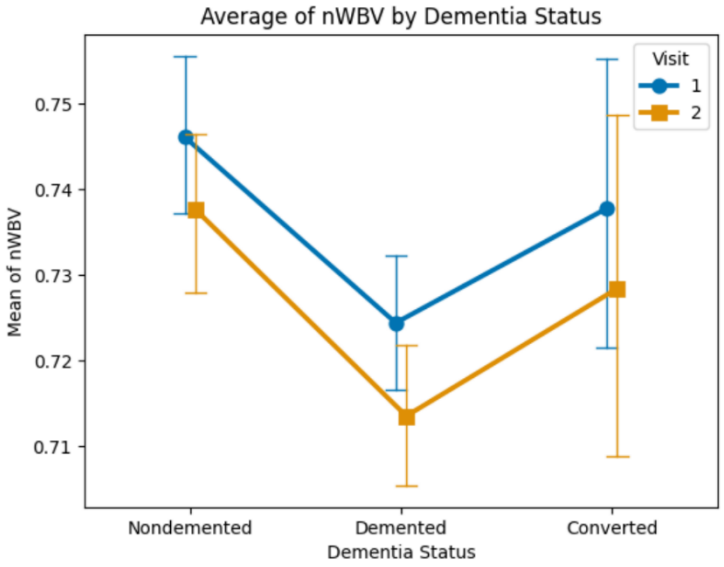

Figure 3. Output plot of nWBV by visit and dementia status.

Dementia Status	Visit	Test Statistic	P-value
Nondemented	1	0.989	0.772
Nondemented	2	0.984	0.511
Demented	1	0.992	0.955
Demented	2	0.979	0.385
Converted	1	0.934	0.341
Converted	2	0.940	0.502

Table 3. Shapiro-Wilk test to check normality of nWBV for each combination of dementia status and visit.

Visit	Test Statistic	P-value
1	1.045	0.354
2	0.299	0.742

Table 4. Levene's test to check homogeneity of variances in nWBV for each visit.

Within-Subjects Effect	P-value
Visit	p > 0.05

Table 5. Mauchly's test of sphericity for nWBV.

Source	df_1	df_2	Sum of Squares	Mean of Squares	F-value	P-value	Effect Size
Dementia Status	2	141	0.034	0.017	6.712	0.002	0.087
Visit	1	141	0.007	0.007	94.251	p < 0.001	0.401
Dementia Status x Visit	2	141	SS < 0.001	MS < 0.001	1.534	0.219	0.021

Table 6. Two-way mixed ANOVA summary table for nWBV.

ASF Analysis

Since the p-value > 0.05 in all three tests: Shapiro-Wilk, Levene, and Mauchly, we can conclude no violations to the following assumptions: ASF is normally distributed for each dementia status and visit, equal variances between dementia status for each visit, and sphericity (see Table 7, Table 8, and Table 9).

The two-way mixed ANOVA summary in Table 10 presents a statistical difference in ASF between the first and second visit at significance level of $\alpha = 0.05$ (F-value = 8.754, p-value = 0.004). Despite this interpretation, the output plot in Figure 4 shows a minor difference in the means of ASF between two visits, especially for the nondemented and converted groups. The reason is most likely due to its small effect size (0.058). Another observation in the output plot is that the mean of ASF between the nondemented and demented groups is close to each other within the same visit. Similarly to the median of ASF, it is surprising to see that the converted group have the highest mean of ASF. Since converted patients started without dementia and ended up getting it, we would expect that their mean of ASF is in between the nondemented and demented group's mean. This is a sign that dementia status does not have a significant effect on ASF, which is supported by the results of the mixed ANOVA test (p-value = 0.792). In addition, there is not enough evidence that the interaction between dementia status and visits impacts ASF (p-value = 0.361).

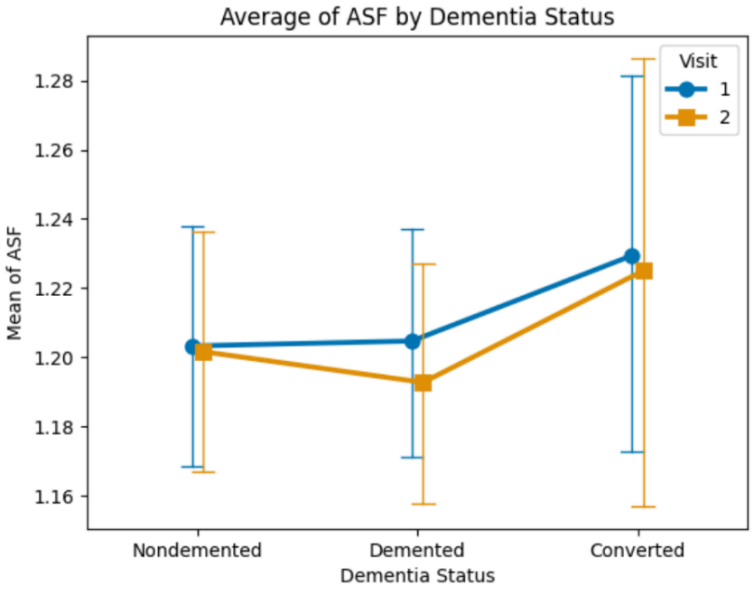

Figure 4. Output plot of ASF by visit and dementia status.

Dementia Status	Visit	Test Statistic	P-value
Nondemented	1	0.990	0.817
Nondemented	2	0.993	0.961
Demented	1	0.986	0.697
Demented	2	0.982	0.519
Converted	1	0.957	0.674
Converted	2	0.932	0.405

Table 7. Shapiro-Wilk test to check normality of ASF for each combination of dementia status and visit.

Visit	Test Statistic	P-value
1	0.879	0.417
2	0.392	0.677

Table 8. Levene's test to check homogeneity of variances in ASF for each visit.

Within-Subjects Effect	P-value
Visit	p > 0.05

Table 9. Mauchly's test of sphericity for ASF.

Source	df_1	df_2	Sum of Squares	Mean of Squares	F-value	P-value	Effect Size
Dementia Status	2	141	0.018	0.009	0.234	0.792	0.003
Visit	1	141	0.003	0.003	8.754	0.004	0.058
Dementia Status x Visit	2	141	0.001	MS < 0.001	1.028	0.361	0.014

Table 10. Two-way mixed ANOVA summary table for ASF.

Power Analysis

During the exploratory data analysis, it was discovered that each dementia status has unequal sample sizes, particularly the number of converted patients is less than half the size of the demented group and the undemented group. It would have been better if a statistical power analysis had been conducted before gathering participants. This would help determine the appropriate sample size for the experiment and reduce the risk of Type II errors. Power curves with low, medium, and high effect sizes are explored as sample size changes between 10 and 200 at a critical threshold of $\alpha = 0.05$ (see Figure 5). If we want to aim for 91% power when the effect size is 0.70 and the significance level is $\alpha = 0.05$, the appropriate sample size for each group should be approximately 46.

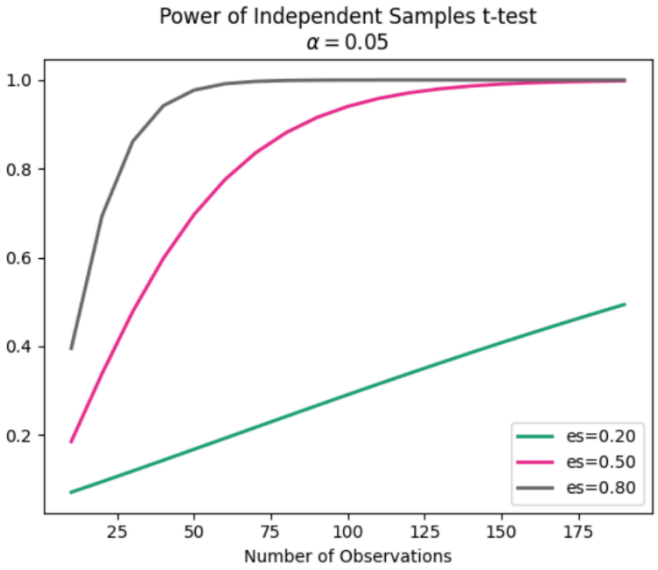

Figure 5. Statistical Power Analysis Plot

Conclusion

In the hope of identifying dementia early for future patients, we used a longitudinal study to compare nWBV and ASF between dementia statuses as MRI visits increase. The quantitative analysis from the two-way mixed ANOVA concludes that the changes in nWBV and ASF are not the result of an interaction between the dementia status and the number of MRI visits. However, there is a significant change in nWBV due to either factor. For ASF, a statistical difference between the first and second visit is found, but dementia status has no significant effect on it. In future work, we can use a multiple linear regression model to predict the changes in nWBV and research treatments that can minimize the symptoms of dementia. If we perform another experiment to examine the effects of treatments, we need to consider power analysis first to determine the appropriate sample size for each group.

References:

Boysen, J. (2017). MRI and Alzheimers. Retrieved from https://www.kaggle.com/datasets/jboysen/mri-and-alzheimers/data

Buckner, R. L., Head, D., Parker, J., Fotenos, A. F., Marcus, D., Morris, J. C., & Snyder, A. Z. (2004). A unified approach for morphometric and functional data analysis in young, old, and demented adults using automated atlas-based head size normalization: reliability and validation against manual measurement of total intracranial volume. *NeuroImage (Orlando, Fla.)*, *23*(2), 724–738. https://doi.org/10.1016/j.neuroimage.2004.06.018

Dementia Statistics. Alzheimer's Disease International. (n.d.). Retrieved from https://www.alzint.org/about/dementia-facts-figures/dementia-statistics/

Division of Population Health. (2019, April). *About Dementia*. Centers for Disease Control and Prevention. Retrieved from https://www.cdc.gov/aging/dementia/index.html

Roe, C. M., Fagan, A. M., Grant, E. A., Marcus, D. S., Benzinger, T. L., Mintun, M. A., Holtzman, D. M., & Morris, J. C. (2011). Cerebrospinal fluid biomarkers, education, brain volume, and future cognition. Archives of neurology, 68(9), 1145–1151. https://doi.org/10.1001/archneurol.2011.192

Starkman, G. (n.d.). *Does A Genius Have A Large Brain?* NY Neurology Associates. Retrieved from https://www.nyneurologists.com/blog/does-a-genius-have-a-large-brain

What is Alzheimer's disease? Alzheimer Society of Canada. (2024). Retrieved from https://alzheimer.ca/en/about-dementia/what-alzheimers-disease